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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/071,505	02/08/2002	Ingrid Henriksen	NIDN-10439	8899

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EXAMINER	
SHARAREH, SHAHNAM J	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 11/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/071,505	HENRIKSEN ET AL.	
	Examiner	Art Unit	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-9,11-17 and 19* is/are pending in the application.

4a) Of the above claim(s) *8,9 and 13-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 5-7, 11-12, 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 8, 2005 has been entered.

Claims 1, 3, 5-9, 11-17, 19 are pending. Claims 8-9, 13-17 stand withdrawn. Claims 1, 3, 5-7, 11-12, 19 are under consideration.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2. Claims 1; 3, 5-7, 11-12, 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unger US Patent 6,033,645.

Unger discloses methods of administering a gaseous contrast agent comprising administering the contrast agent and a flushing agent from two different vessels into tubing that enters an upper extremity of a patient. (see figures 1-2; abstract, col 6, line 49-col 7, line 20; col 53, lines 35-67). The rates of infusion of Unger fall within the scope of the instant limitation of claim 1, "controllably," because it falls within the ranges that are described by Unger (see col 44-47). Unger claims delivery of his contrast agent in a continuous infusion (col 64, lines 20-29). The position of the syringe carrying the contrast agent in Unger is vertical (see figure 1). Unger uses the piston of the syringe as the driver (see element 18 of figure 1).

The flushing agent of Unger is normal saline (col 49, lines 53-55; col 57, line 9). The flushing step of Unger allows complete transport of the gaseous contrast agent into the bloodstream; thus, at least a portion of the contrast agent of Unger is mixed with the flushing agent of Unger prior to administration into the subject. (col 47, lines 60-col 48,

line 10). Unger further explicitly teaches flush rates that fall within the scope of the instant claim 19 (col 48, line 64-col 49, line 25).

Unger claims administration of sulfur hexafluoride and perfluorocarbon filled vesicles such as perflurobutane as his contrast agent (see examples, also col 57, lines 9-21). The vesicles of Unger include albumin-stabilized microbubbles (see col 35, line53-col 36, line 30). Thus, limitations of claims 5-7, 11-12 are also met.

Even though, Unger fails to explicitly recite the instantly claimed infusion period of 5-60 minutes, he explicitly places one of ordinary skill in the art at notice that the rate of administration can be optimized based on the volume of the composition, gaseous vesicles, type of encapsulation and other patient variable such as age, area of interest, etc... Unger makes such statements at numerous places in his patent. For example, Unger at col 45 states:

> The compositions may be administered over a period of time which can vary and depends upon a variety of factors including, for example, the volume of the composition being administered, the age and weight of the patient, the particular materials employed in the compositions, including, for example, lipids, polymers, proteins, vesicles, gases and/or gaseous precursors, the purpose for the administration (for example, diagnostic or therapeutic), the region of interest, the mode of administration, the size of the vesicles (in the case of vesicle compositions), and the like. An exemplary administration time for the compositions described above is about 5 seconds. Dividing the gas dose by this time period provides a gas administration rate which can be expressed as cc gas/Kg-sec. Thus, a gas dose of, for example, about 1×10^{-4} cc gas/Kg and an administration time of 5 sec provides a gas administration rate of about 2×10^{-5} cc gas/Kg-sec.
>
> It is to be understood that the foregoing specific gas concentrations, composition doses, administration times and administration rates are for purposes of illustration only, and not for purposes of limitation.

Note that Unger states that any exemplified rate is for purposes of illustration not for purposes of limitation. (see col 45, lines 25-28).

At col 47 Unger explicity states that

> As would be apparent to one skilled in the art, based on the present disclosure, the rate at which the lipid and/or vesicle compositions are preferably administered can vary, depending, for example, on the lipids, polymers, proteins, vesicles, gases and/or gaseous precursors employed, the age and weight of the patient, the mode of administration, the size of the vesicles (in the case of vesicle compositions), and the like. Typically, administration may be carried out at lower rates and the rate can be increased until a desired effect is achieved.

Thus, as encouraged by Unger modifying the rate of administration to observe a desired clinical effect is within the scope of the teaching of Unger

Subsequently, absent a showing of unexpected results, it would have been obvious to one of ordinary skill in the art at the time of invention to optimize the rate of administration of the contrast agent of Unger by routine experimentations and enhance the quality of images, because Unger explicitly recites the rate dependent factors. Thus, one of ordinary skill in the art would have had a reasonable expectation of success in achieving optimal images by determining the optimal rate of infusion.

Response to Arguments

3. Applicant's arguments with respect to the rejected claims have been considered but are persuasive.

Applicant has argued that the contrast agent of Unger is typically administered over a period of 5 seconds to 50 seconds (Response at page 7, 1st para). As pointed above, Unger explicitly disclaims any specific rates to be the exhaustive rate limitation. Unger further elaborates on factors that determine the ultimate rate. Accordingly, modifications of the rate of administration would have been well within the purview of one of ordinary skill in the art.

Applicant also argues that Unger's reference to "continuous infusion" is directed to the administration of the flushing medium, not the contrast agent. (see *Id.*). In response, Examiner cannot find applicant's scientific or legal rational for such interpretation. Unger clearly states that his composition comprising the contrast agent is administered by continuous infusion (see col 64, lines 25-28). Unger further describes the scope of the term "administration" at col 9, lines 4-10 to include both the

administration of the composition and/or the flushing agent. Finally, Unger elaborates on a suitable rate of administration. Thus, Applicant's arguments are not persuasive.

Applicant then argues that Unger's mode of administration and positioning of the delivery vessel are merely incidentally overlap with the scope of the instant claims and there is no evidence that Unger's method would enhance product homogeneity (see Arguments at page 7, 2nd para.). In response, Examiner states that since Unger teaches all elemental steps of the instant claims, the intended purpose of the claims are also achieved. Further, whether Unger incidentally teaches the instantly claimed mode of administration is irrelevant, because irrespective of Unger's intention, the elemental steps of the instant claims are described by Unger.

Conclusion

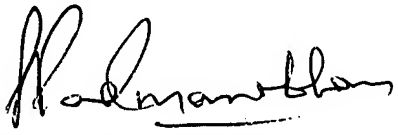
4. No claims are allowed.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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